

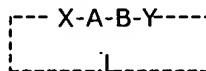
AMENDMENTS TO THE CLAIMS

Please amend claims 1, 2, 4-9, 12, 13, 15, 18-28, 31-39, 42-53, 55-104, 106-113, and 138-162, and cancel claims 3, 10, 11, 14, 16, 17, 29, 30, 40, and 114-137, as shown in the following listing of claims, which will replace all prior versions and listings of claims in the application. Claims 1, 2, 4-9, 12, 13, 15, 18-28, 31-113, and 138-162 are pending in the application. Claims 3, 10, 11, 14, 16, 17, 29, 30, 40, and 114-137 are canceled without prejudice to their pursuit in an appropriate continuation or divisional application.

In the claims:

1 (currently amended). A compound having the general formula I

(I)



where the dashed line indicates that formula I is optionally cyclic, and the bonds shown represent covalent bonds;

and wherein A represents a chemical moiety having an amino group (radical) and a carboxy group that forms part of the peptide bond connecting A to X and B;

B represents a chemical moiety having an amino group (radical) and a carboxy group that forms part of the peptide bond connecting B to A and Y;

X represents a peptide sequence of from 1 to 3 amino acid residues which independently may be an L or D form when Y represents a C-terminal peptide sequence of from 2 to 5 amino acid residues which may independently be L- or D-forms;

or X represents an N-terminal modification of the group A-B when Y represents a C-terminal peptide sequence of from 2 to 5 amino acid residues which may independently be L- or D-forms; or

X represents a peptide sequence of from 2 to 5 amino acid residues which may independently be L- or D-forms when Y represents a C-terminal peptide sequence of from 1 to 3 amino acid residues which independently may be an L or D form;

and when formula I represents a linear peptide X is optionally chemically modified at its N-terminal,

and L is an optional linking group comprising from 0 to 8 backbone atoms;

and a mirror image or a retro analogue of formula I, or a derivative of formula I which is a pharmaceutically acceptable salt, an alkyl, aryl or aralkyl ester, an amide, a mono or disubstituted amide where the substituent is an alkyl, an aryl or an aralkyl, a hydrazide, or an alcohol;

~~with the proviso that the compounds~~

with the proviso that the compounds

(SEQ ID NO: 41) H-Gly-Pro-Leu-Gly-Pro-OH,

(SEQ ID NO: 42) H-Pro-4Hyp-Gly-Ala-Gly-OH,

(SEQ ID NO: 43) N-3-(4-hydroxyphenyl)propionyl-Pro-4Hyp-Gly-Ala-Gly-OH,

(SEQ ID NO: 44) N-3-phenylpropionyl-Pro-4Hyp-Gly-Ala-Gly-OH,

(SEQ ID NO: 45) N-3-phenylpropyl-Pro-4Hyp-Gly-Ala-Gly-OH,

N-3-(4-hydroxyphenyl)propionyl-Pro-4Hyp-Gly-Ala-OH,

N-3-(4-hydroxyphenyl)propionyl-Pro-4Hyp-Gly-OH,

N-3-(4-hydroxyphenyl)propionyl-Pro-4Hyp-OH,

(SEQ ID NO: 46) N-3-(4-hydroxyphenyl)propionyl-Pro-Pro-Gly-Ala-Gly-OH,

(SEQ ID NO: 47) H-Gly-Ala-Gly-4Hyp-Pro-Tyr-NH₂,

(SEQ ID NO: 48) H-Gly-Ala-Gly-4Hyp-Pro-Tyr-OH,

(SEQ ID NO: 49) H-Ala-Gly-4Hyp-Pro-Tyr-NH₂,

(SEQ ID NO: 50) H-Gly-Sar-Pro-Gly-Ala-Gly-OH,

(SEQ ID NO: 51) H-Gly-Pro-Sar-Gly-Ala-GlyOH,

(SEQ ID NO: 52) H-Gly-Sar-Sar-Gly-Ala-Gly-OH,

(SEQ ID NO: 53) H-Gly-Ala-Gly-Hyp-Pro-Tyr(3-I)-NH₂,

(SEQ ID NO: 54) H-Gly-Ala-Gly-Hyp-Pro-Tyr(3-F)-NH₂

(SEQ ID NO: 55) H-Gly-Ala-Gly-Hyp-Pro-Tyr(3-Cl)-NH₂

(SEQ ID NO: 56) H-Gly-Ala-Gly-Hyp-Pro-Tyr(3-Br)-NH₂

(SEQ ID NO: 57) H-Arg-Ala-Gly-Hyp-Pro-Tyr-NH₂

(SEQ ID NO: 58) H-Val-Ala-Gly-Hyp-Pro-Tyr-NH₂

(SEQ ID NO: 59) H-Ala-Ala-Gly-Hyp-Pro-Tyr-NH₂

(SEQ ID NO: 60) H-Gly-Ala-Gly-Hyp-His-Tyr-NH₂

(SEQ ID NO: 61) H-Gly-Ala-Gly-Hyp-Pro-Phe-NH₂

(SEQ ID NO: 62) Cyclo(CF₃C(OH)-Gly-Ala-Gly-4Hyp-Pro-Tyr-CONH), and

(SEQ ID NO: 63) Cyclo(CO-Gly-Ala-Gly-4Hyp-Pro-Tyr-CONH).

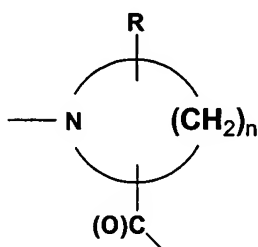
are not covered by the general formula I.

2 (currently amended). ~~The~~The compound according to claim 1 wherein said covalent bonds are selected from peptide bonds, disulphide bonds, ester bonds, reduced amide bonds, alkoxy bonds, oxycarbonyl bonds, and acyloxyalkoxy bonds.

3 (canceled).

4 (currently amended). ~~The~~A compound according to ~~any one of the preceding claims 1,~~ wherein A and B each represents an amino acid or an amino acid derivative having functional amino and carboxy groups.

5 (currently amended). ~~The~~A compound according to ~~any one of claims 1 to 4,~~ wherein A-B represents a dipeptide selected from the group consisting of Sar-Sar, Sar-Hyp, Hyp-Sar, Pro-Sar, Sar-Pro, Pro-Hyp, Pro-Pro, Hyp-Pro, and Hyp-Hyp, where Pro and Hyp independently may be an L or D form, where the ring structure of Pro and Hyp is optionally substituted with halogen, nitro, methyl, amino, or phenyl, and Hyp represents 3-hydroxyproline or 4-hydroxyproline, or one or both of the amino acid residues of A-B is a Sar, or N-cyclohexylglycine residue.

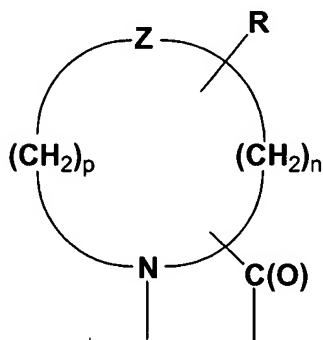


6 (currently amended). ~~The~~A compound according to ~~any one of claims 1 to 3,~~ wherein the groups A and B each independently represents a group of the formula II

(II)

wherein n is an integer having the value 3, 4, or 5, and R represents an optional substituent, preferably selected from the group consisting of halogen, phenyl, hydroxy, NH₂, and C(1-6)alkyl optionally substituted with halogen.

7 (currently amended). ~~The~~A compound according to ~~any one of claims 1 to 3,~~ wherein the groups A and B are represented by the formula IIa



IIa

Wherein n is an integer having the value 0, 1, 2, and 3, p is an integer having the value 0, 1, 2, and 3, Z represents O or S, and R represents an optional substituent, preferably selected from the group consisting of halogen, phenyl, hydroxy, NH₂, and C(1-6)alkyl.

8 (currently amended). ~~The~~A compound according to ~~any one of the two preceding claims 1,~~ wherein R is selected from the group consisting of F, Cl, Br, phenyl, OH, NH₂, CH₃, and CF₃.

9 (currently amended). ~~The~~A compound according to ~~any one of the preceding claims 1,~~ wherein A and B independently represents an amino acid residue having a saturated carbocyclic structure of 4, 5 or 6 members and where in said carbocyclic structure further comprises one or more heteroatoms.

10. – 11. (canceled)

12 (currently amended). ~~The~~A compound according to ~~any one of claims 6 and 7,~~ wherein A and B is selected from the group consisting of N- and C(O)- radicals of the following compounds:

D/L-azetidin-3-carboxylic acid,

D/L-azetidin-2-carboxylic acid,

D/L-Indolin-2-carboxylic acid,

D/L-1,3-dihydro-isoindol-1-carboxylic acid,
D/L-thiazolidin-4-carboxylic acid,
D/L-pipecolinic acid,
D/L-Nipecotinic acid,
Isonipecotinic acid,
L/D-2-carboxymorpholin,
L/D-1,2,3,4-tetrahydroquinolin-3-carboxylic acid,
L/D-1,2,3,4-tetrahydroquinolin-3-carboxylic acid, and
4-carboxy-4-phenyl-piperidin.

13 (currently amended). ~~The~~A compound according to ~~any one of the preceding claims 1,~~ wherein formula I represents a linear peptide wherein said chemical modification of the N-terminal of X is
an acylation with an optionally substituted straight, branched, saturated, unsaturated, or aromatic C(1-22)carboxylic acid where the substituent is selected from hydroxy, halogen, C(1-6)alkyl, nitro or cyano and may be situated on the carbon chain or the aromatic moiety.

14 (canceled).

15 (currently amended). ~~The~~A compound according to ~~any one of the preceding claims 1,~~ wherein formula I represents a linear peptide wherein said chemical modification of the N-terminal of X is
an alkylation with an optionally substituted C(1-22)alkyl or aryl C(1-22)alkyl where the substituent is selected from hydroxy, halogen, C(1-6)alkyl, nitro or cyano and may be situated on the carbon chain or the aromatic moiety.

16. – 17. (canceled)

18 (currently amended). ~~The~~A compound according to claim 15, wherein X represents one amino acid residue.

19 (currently amended). ~~The~~A compound according to the ~~preceding claim 1,~~ wherein said amino acid residue is selected from the group consisting of L-Tyr and D-Tyr optionally acylated with a C(1-4)carboxylic acid when Y represents a C-terminal peptide sequence of from 2 to 5 amino acid residues as defined in claim 1.

20 (currently amended). TheA compound according to the preceding claim 1 wherein said C(1-4)carboxylic acid is acetic acid.

21 (currently amended). TheA compound according to ~~any one of claims 1-12 to 20~~, wherein A-B is selected from the group consisting of Pro-Hyp, Pro-Pro, Hyp-Pro, and Hyp-Hyp where Pro and Hyp independently may be an L or D form.

22 (currently amended). TheA compound according to the preceding claim 1, wherein Hyp represents L-4Hyp.

23 (currently amended). TheA compound according to ~~any one of claims 12 to 22~~, wherein Y represents a peptide of 3 or 4 amino acid residues being independently L- or D-forms.

24 (currently amended). TheA compound according to the preceding claim 1, having Sar or Gly at its C-terminal.

25 (currently amended). TheA compound according to ~~any one of claims 18 to 27~~ 1, wherein Y represents a peptide sequence selected from the group consisting of

Gly-L-Ala-Gly,

Gly-L-Ala-Gly,

Gly-D-Ala-Gly,

Gly-D-Ala-Gly, and

Sar-Aib-Sar.

26 (currently amended). TheA compound according to ~~any one of claims 1, to 11~~ wherein formula I represents a linear peptide and X represents an N-terminal modification of the group A-B.

27 (currently amended). TheA compound according to the preceding claim 1, wherein said modification is an acylation of the N-terminal of A-B with a compound selected from the group consisting of phenylpropionic acid and derivatives thereof; phenylacetic acid and derivatives thereof; phenoxyacetic acid and derivatives thereof; benzoylglycine and derivatives thereof; and phenylglycine and derivatives thereof.

28 (currently amended). TheA compound of formula I selected from the group consisting of (SEQ ID NO: 69) Ac-L-Tyr-L-Pro-L-4Hyp-Gly-L-Ala-Gly,

Ac-D-Tyr-D-Pro-D-4Hyp-Gly-D-Ala-Gly,

A portion of various compounds 4HPPA-L-Pro-L-4Hyp-Gly-L-Ala-Gly, and a pharmaceutically acceptable salt, an alkyl ester, an amide, an alkylamide, an aryl amide, a dialkylamide, an aryl/alkyl amide, a hydrazide, or an alcohol thereof.

29. – 30. (canceled)

31 (currently amended). ~~The~~a compound according to the preceding claim wherein A-B is selected from the group consisting of Pro-Hyp, Pro-Pro, Hyp-Pro, and Hyp-Hyp where Pro and Hyp independently may be an L or D form and Hyp preferably represents 4-hydroxyproline.

32 (currently amended). ~~The~~a compound according to ~~the preceding claim 1,~~ wherein A-B represents unsubstituted L-Pro-L-4Hyp, L-4Hyp-L-Pro, D-Pro-D-4Hyp, or D-4Hyp-D-Pro.

33 (currently amended). ~~The~~A compound according to ~~any one of claims 31 to 34~~ 1, wherein X represents a single amino acid residue.

34 (currently amended). ~~The~~A compound according to ~~the preceding claim 1,~~ wherein X represents L-Tyr or D-Tyr optionally further substituted with halogen, phenyl, hydroxy, NH₂, C(1-6)alkoxy, aryloxy, and C(1-6)alkyl optionally substituted with halogen, at its aromatic ring when Y represents a peptide of 3 or 4 amino acid residues being independently L- or D-forms.

35 (currently amended). ~~The~~A compound according to ~~the preceding claim 1,~~ wherein Y has Asp, Asn, Gln or Glu at its C-terminal.

37 (currently amended). ~~The~~A compound according to ~~the preceding claim 1,~~ wherein Y represents a peptide sequence selected from the group consisting of

Gly-L-Ala-L-Asn,

Gly-D-Ala-L-Asn,

(SEQ ID NO: 166) Gly-L-Ala-Gly-L-Asn,

Gly-L-Ala-Gly-D-Asn,

Gly-L-Ala-L-Gln,

(SEQ ID NO: 167) Gly-L-Ala-Gly-L-Gln,

Gly-L-Ala-Gly-D-Gln,

Gly-D-Ala-D-Asn,

Gly-D-Ala-Gly-D-Asn,
 Gly-D-Ala-Gly-L-Asn,
 Gly-D-Ala-D-Gln,
 Gly-D-Ala-Gly-D-Gln,
 Gly-D-Ala-L-Gln,
 Gly-D-Ala-Gly-D-Gln,
 Gly-L-Ala-L-Asp,
 Gly-D-Ala-L-Asp,
 (SEQ ID NO: 168) Gly-L-Ala-Gly-L-Asp,
 Gly-L-Ala-Gly-D-Asp,
 Gly-L-Ala-L-Glu,
 (SEQ ID NO: 169) Gly-L-Ala-Gly-L-Glu,
 Gly-L-Ala-Gly-D-Glu,
 Gly-D-Ala-D-Asp,
 Gly-D-Ala-Gly-D-Asp,
 Gly-D-Ala-Gly-L-Asp,
 Gly-D-Ala-D-Glu,
 Gly-D-Ala-Gly-D-Glu,
 Gly-D-Ala-L-Glu,
 Gly-D-Ala-Gly-D-Glu.

38 (currently amended). TheA compound according to claim 1, -wherein X represents a peptide sequence selected from the group consisting of

Gly-L-Ala-L-Asp,
 (SEQ ID NO: 170) Gly-L-Ala-Gly-L-Asp,
 Gly-L-Ala-L-Glu,
 (SEQ ID NO: 171) Gly-L-Ala-Gly-L-Glu,
 Gly-D-Ala-D-Asp,
 Gly-D-Ala-Gly-D-Asp,
 Gly-D-Ala-D-Glu,
 Gly-D-Ala-Gly-D-Glu,
 and Y represents a single amino acid residue.

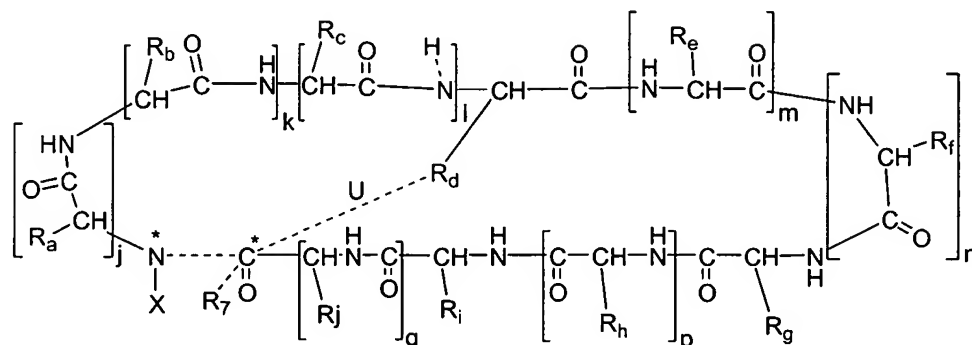
39 (currently amended). TheA compound according to the preceding claim 1, wherein Y represents L-Tyr or D-Tyr optionally further substituted with halogen, phenyl, hydroxy, NH₂,

C(1-6)alkoxy, aryloxy, and C(1-6)alkyl optionally substituted with halogen, at its aromatic ring.

40 (canceled).

41 (original). A compound of the general formula XII

(XII)



representing a peptide sequence wherein the amino acid residues may be D- and/or L-forms, and having the N-terminal at N* and the C-terminal at C* and being optionally cyclic via a covalent bond between N* and C* as shown by a broken line or between R_d and C* as shown by the broken line U; and wherein

X represents an N-terminal moiety such as a photoprobe capable of being bond to the amino terminal N*, or an acyl group derived from a C(2-22)alkyl carboxylic acid, such as acetic acid, propionic acid, butyric acid and other fatty acids, such as behenic acid, optionally substituted with one or more substituents selected from the group consisting of hydroxy, halogen, C(1-6)alkyl, nitro and cyano; or X represents hydrogen;

R₇ represents OH, NH₂, NHHN₂ or OR₈ when the bond between N* and C* is missing, or R₇ is absent when there is a bond between N* and C*;

R₈ represents H or a straight or branched C(1-6)alkyl group, an aryl or an aralkyl group.

R_a represents the amino acid side chain of Hyp or Pro;

R_b represents the amino acid side chain of Hyp or Pro;

R_c represents the amino acid side chain of Gly, Sar, an aromatic amino acid side chain optionally substituted with one or more hydroxy, halogen or lower alkoxy group in the aromatic ring;

R_d represents the amino acid side chain of Ala, Gly, Glu, Asp, Dab, Dapa, Lys, Asn, Gln, Orn, or Cys;

R_e represents the amino acid side chain of Ala;

R_f represents the amino acid side chain of Ala, Sar or Gly;

R_g represents any amino acid side chain except the side chain of L-4Hyp or a moiety of formula II or Iia;

R_h represents the amino acid side chain of Ala, or R_g represents a moiety of formula II or Iia;

R_i represents the amino acid side chain of Gly or R_i represents an aromatic amino acid optionally substituted with one or more halogen groups in the aromatic ring;

R_j represents Asn, Gln, Asp, Glu, Cys or Tyr;

and each of j, k, l, m, n, p and q is independently 0 or 1;

and the retro form, all D form, or retro all-D form of the peptide sequence of formula XII, and salts and amides thereof.

42 (currently amended). ~~The~~A compound according to the preceding claim 41 wherein X is selected from the group consisting of Ac and the photoprobes ASAL optionally iodinated in position 5 to yield the group 2-hydroxy-4-azido-5-iodo benzoyl, and AB.

43 (currently amended). ~~The~~A compound according to any one of the two preceding claims 41, wherein R₇ is NH₂.

44 (currently amended). ~~The~~A compound according to any one of the three preceding claims 41, wherein R_a is the amino acid side chain of Pro.

45 (currently amended). ~~The~~A compound according to any one of the four preceding claims 41, wherein R_b is the amino acid side chain of Hyp.

46 (currently amended). ~~The~~A compound according to any one of the five preceding claims 41, wherein R_c is the amino acid side chain of Gly or Tyr.

47 (currently amended). ~~The~~A compound according to any one of the six preceding claims 41, wherein R_d is selected from the group consisting of the amino acid side chain of Gly, Asp or Glu, Dapa and Dab.

48 (currently amended). ~~The~~A compound according to any one of the seven preceding claims 41 wherein R_f is Ala or Gly.

49 (currently amended). ~~The~~A compound according to any one of the eight preceding claims 41, wherein R_g is the amino acid side chain of Pro, Asn or Gly.

50 (currently amended). ~~The~~A compound according to ~~the preceding claim 1~~, wherein R_g is the amino acid side chain of Asn, Gly, D-4Hyp or L-/D-Pro when formula XII represents a linear peptide, or when formula XII represents a peptide cyclised between N^* and C^* then R_g represents the amino acid side chain of L-/D-4Hyp or L-/D-Pro.

51 (currently amended). ~~The~~A compound according to ~~any one of the ten preceding claims 1~~ wherein R_h is the amino acid side chain of Ala when U is missing, or R_h is Pro or Hyp when U is present.

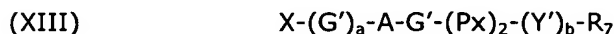
52 (currently amended). ~~The~~A compound according to ~~any one of the eleven preceding claims 41~~, wherein R_i is preferably Tyr, Phe, Trp, Nal optionally substituted with one or more hydroxy, F or Cl, in the aromatic ring.

53 (currently amended). ~~A~~~~The~~ compound according to ~~any one of the twelve preceding claims 41~~, wherein R_j is selected from the group consisting of the amino acid side chain of Asp, Glu, and Tyr.

54 (original). A linear peptide according to claim 41 of formula XII which is an retro all-D form.

55 (currently amended). ~~A~~~~The~~ ~~peptide~~ compound according to claim 1 of formula XII consisting of between 3 and 9 amino acid residues, more preferably between 3 and 7 amino acid residues and wherein j and k are preferably 0 when U is present, j and k are preferably 1 when U is missing and formula XII represents a cyclic peptide, m is preferably 0 when U is missing, p is preferably 1 when U is present, and q is preferably 0 when U is present.

56 (currently amended). ~~A~~~~The~~ compound according to claim 1 or 41 and having the general formula XIII



specifying a peptide sequence wherein the amino acid residues may be L and/or D forms, and wherein

X represents H or Ac;

G' represents a glycine residue or a glycine analogue such as Sar;

A represents alanine;

Px represents an amino acid residue of formula II or IIa such as Hyp or Pro;

Y' represents tyrosine or phenylalanine optionally substituted in the phenyl ring with halogen or hydroxy;

a and b are independently 0 or 1,

R₇ represents OH, NH₂, NHHNH₂, Asn-NH₂, or Gln-NH₂;

and retro forms thereof and salts thereof.

57 (currently amended). ~~The~~A compound according to ~~the preceding claim 56~~, wherein X represents Ac and all amino acid residues are L-forms.

58 (currently amended). ~~The~~A compound according to ~~any one of the two preceding claims 56~~, wherein G' is glycine.

59 (currently amended). ~~The~~A compound according to ~~any one of the three preceding claims 56~~, wherein Px is Pro.

60 (currently amended). ~~The~~A compound according to ~~any one of the four preceding claims 56~~, wherein Y' is Tyr.

61 (currently amended). ~~The~~A compound according to ~~any one of the five preceding claims 56~~, wherein R₇ is NH₂.

62 (currently amended). ~~The A-retro~~ compound of formula XIII having the formula XIIIa: X-(Y')_b-(Px)₂-G'-A-(G')_a-R₇ wherein all amino acid residues are D-forms and wherein all symbols have the same meaning as defined above for formula XIII and wherein the compound is retro.

63 (currently amended). ~~The A-peptide~~ compound of formula XIII, wherein at least one Px residue is a D-amino acid and the rest are L-amino acids.

64 (currently amended). ~~The compound A-cyclic-sequence~~ of formula XIII, wherein the compound is cyclic and wherein X represents H, R₇ represents Asn or Gln having a covalent bond to Y' which represents Tyr, b is 1, and a is 1.

65 (currently amended). ~~AA~~-compound having the of formula 2: H-GAG-(Pa)₂-NH₂ as defined herein or a salt thereof.

66 (currently amended). ~~The~~A compound according to the ~~preceding~~ claim 65 selected from the group consisting of

H-Gly-Ala-Gly-D-Hyp-Pro-Tyr-NH₂,

H-Gly-Ala-Gly-D-Pro-Pro-Tyr-NH₂,

H-Gly-Ala-Gly-D-Pro-Ala-Tyr-NH₂,

H-Gly-Ala-Gly-Gly-D-Pro-Tyr-NH₂,

H-Gly-Ala-Gly-D-Hyp-Ala-Tyr-NH₂,

H-Gly-Ala-Gly-D-Hyp-D-Pro-Tyr-NH₂, and pharmaceutically acceptable salts thereof.

67 (currently amended). AA-compound having the ~~of~~ formula 3: H-GAG-(Px)₂-Y-NH₂ as defined herein or a salt thereof.

68 (currently amended). ~~The~~A-compound according to the ~~preceding~~ claim 67 selected from the group consisting of

(SEQ ID NO: 64) H-Gly-Ala-Gly-NCG-Pro-Tyr-NH₂,

(SEQ ID NO: 65) H-Gly-Ala-Gly-T4C-Pro-Tyr-NH₂,

(SEQ ID NO: 66) H-Gly-Ala-Gly-A2C-Pro-Tyr-NH₂,

(SEQ ID NO: 67) H-Gly-Ala-Gly-PC-Pro-Tyr-NH₂, and pharmaceutically acceptable salts thereof.

69 (currently amended). A compound having the ~~of~~ formula 8: H-G'-A-G'-(Px)₂-Y-NH₂ as defined herein or a salt thereof.

70 (currently amended). ~~The~~A compound according to the ~~preceding~~ claim 69 selected from the group consisting of H-Sar-Ala-Sar-Hyp-Pro-Tyr-NH₂,

(SEQ ID NO: 281) H-Gly-Ala-Sar-Hyp-Pro-Tyr-NH₂, and pharmaceutically acceptable salts thereof.

71 (currently amended). A compound having the ~~of~~ formula 6: X-G-D-A-G-(D-Px)₂-D-Y-NH₂ as defined herein and salts thereof.

72 (currently amended). ~~The~~A compound according to the preceding claim selected from the group consisting of

H-Gly-D-Ala-Gly-D-Hyp-D-Pro-D-Tyr-NH₂,

H-Gly-D-Ala-Gly-D-Hyp-D-Pro-D-Tyr-D-Asp-OH,

~~Ac-D-Tyr-D-Pro-D-Hyp-Gly-D-Ala-Gly-NH₂~~

Ac-D-Tyr(3,5-di-I)-D-Pro-D-Hyp-Gly-D-Ala-Gly-NH₂,
 Ac-D-Tyr(phenyl ring mono-iodo substituted)-D-Pro-D-Hyp-Gly-D-Ala-Gly-NH₂,
 Ac-D-Tyr-D-Pro-D-Hyp-(12,13C,15N-Gly)-D-Ala-(1,213C,15N-Gly)-NH₂, and pharmaceutically acceptable salts thereof.

73 (currently amended). A ~~A~~ compound having the ~~of~~ formula 9: X-(Y)_p-(Px)₂-GAG-NH₂ as defined herein and salts thereof.

74 (currently amended). ~~The~~A compound according to the preceding claim selected from the group consisting of

(SEQ ID NO: 282) ASAL-Pro-Hyp-Gly-Ala-Gly-NH₂,

(SEQ ID NO: 283) ASAL(mono-iodo substituted)-Pro-Hyp-Gly-Ala-Gly-NH₂,

(SEQ ID NO: 284) AB-Tyr-Pro-Hyp-Gly-Ala-Gly-NH₂,

(SEQ ID NO: 285) AB-Tyr(3,5-di-I)-Pro-Hyp-Gly-Ala-Gly-NH₂, and pharmaceutically acceptable salts thereof.

75 (currently amended). A ~~compopund~~ compound having the ~~of~~ formula 10: Cyclo(-GAG-(Px)₂-Y-N/Q-) as defined herein and salts thereof.

76 (currently amended). ~~The~~A-compound according to the preceding claim selected from the group consisting of

(SEQ ID NO: 286) cyclo(-Gly-Ala-Gly-Hyp-Pro-Tyr-Gln-),

(SEQ ID NO: 287) cyclo(-Gly-Ala-Gly-Hyp-Pro-Tyr-Asn-),

(SEQ ID NO: 288) cyclo(-Gly-Ala-Gly-Pro-Pro-Tyr-Asn-), and pharmaceutically acceptable salts thereof.

77 (currently amended). A compound having the ~~of~~ formula 11: Cyclo(-Y-(Px)₂-GA-(G)_q-N/Q-) as defined herein and salts thereof.

78 (currently amended). ~~The~~A compound according to the ~~preceeding~~ claim 77 selected from the group consisting of

(SEQ ID NO: 289) Compound 3 cyclo(-Tyr-Pro-Hyp-Gly-Ala-Gly-Asn-),

(SEQ ID NO: 290) Compound 4 cyclo(-Tyr-Pro-Hyp-Gly-Ala-Asn-),

(SEQ ID NO: 291) cyclo(-Tyr(3-I, 5-I)-Pro-4Hyp-Gly-Ala-Gly-Asn), and pharmaceutically acceptable salts thereof.

79 (currently amended). A compound having the of formula 12: X-Zd-G(N/Q)Y-NH₂ as defined herein and salts thereof.

80 (currently amended). TheA-compound according to ~~the preceding claim~~ 79 selected from the group consisting of

(SEQ ID NO: 292) H-Gly-Ala-Gly-Asn-Tyr-NH₂,

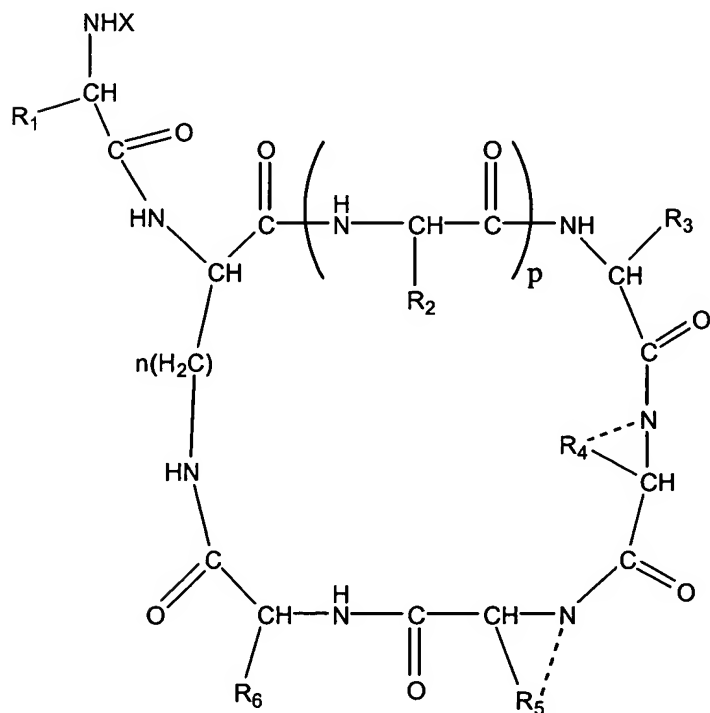
Ac-Gly-Asn-Tyr-NH₂,

H-Gly-Asn-Tyr-NH₂,

(SEQ ID NO: 293) Ac-Ala-Gly-Asn-Tyr-NH₂,

(SEQ ID NO: 294) H-Ala-Gly-Asn-Tyr-NH₂, and pharmaceutically acceptable salts thereof.

81 (currently amended). The compound A ~~cyclic peptide compound of formula XII as defined in claim 41,~~ further characterised in having the general formulae XIV:



XIV


wherein

X represents H or an N-terminal moiety such as a photoprobe capable of binding to the N terminal or an acylation with a C(2-22)alkyl carboxylic acid, such as acetic acid, propionic acid,

butyric acid and other fatty acids such as behenic acid, being optionally substituted with one or more substituents selected from the group consisting of hydroxy, halogen, C(1-6)alkyl, nitro and cyano;

R₁ represents H or CH₃;

R₂ and R₃ are different or the same and represent any possible amino acid side chain;

 represents an optional bond;

R₅ and R₄ represent any possible amino acid side chain or when the optional bond is present R₅ and R₄ represent together with the attached C and N atoms a proline ring which is optionally substituted with OH, preferably in the 4-position, or R₅ and R₄ represent together with the attached C and N atoms a moiety of formula II or IIa above;

R₆ represents an aromatic amino acid side chain optionally substituted in the aromatic ring with one or more substituents selected from halogen, nitro and hydroxy;

p is 0 or 1;

n is 1, 2, 3 or 4;

and salts thereof.

82 (currently amended). ~~The~~A compound according to ~~the preceding claim 81~~, wherein X represents H or the photoprobe groups AB or ASAL₁ which is optionally iodinated as described herein.

83 (currently amended). ~~The~~A compound according to ~~any one of the two preceding claims 81~~, wherein R₁ represents H.

84 (currently amended). ~~The~~A compound according to ~~any one of the three preceding claims 81~~, wherein R₂ and R₃ are different or the same and represent H or CH₃.

85 (currently amended). ~~The~~A compound according to ~~any one of the four preceding claims 81~~, wherein R₅ and R₄ represent together with the attached C and N atoms Pro or Hyp.

86 (currently amended). ~~The~~A compound according to ~~any one of the five preceding claims 81~~, wherein R₆ represents Tyr.

87 (currently amended). ~~The~~A compound according to ~~any one of the six preceding claims 81~~, wherein p is 1.

88 (currently amended). ~~The~~A compound according to ~~any one of the seven preceding claims~~ 81, wherein n is 1.

89 (currently amended). ~~The~~A compound according to claim 81 of formula XIV selected from the group consisting of

(SEQ ID NO: 246)

H-Gly-Dapa-Gly-Hyp-Pro-Tyr

(SEQ ID NO: 247)

H-Gly-Dab-Gly-Hyp-Pro-Tyr

(SEQ ID NO: 248)

H-Gly-Dab-Ala-Gly-Hyp-Pro-Tyr

(SEQ ID NO: 249)

H-Gly-Dapa-Ala-Gly-Hyp-Pro-Tyr

H-Gly-D-Dapa-Gly-D-Hyp-D-Pro-D-Tyr

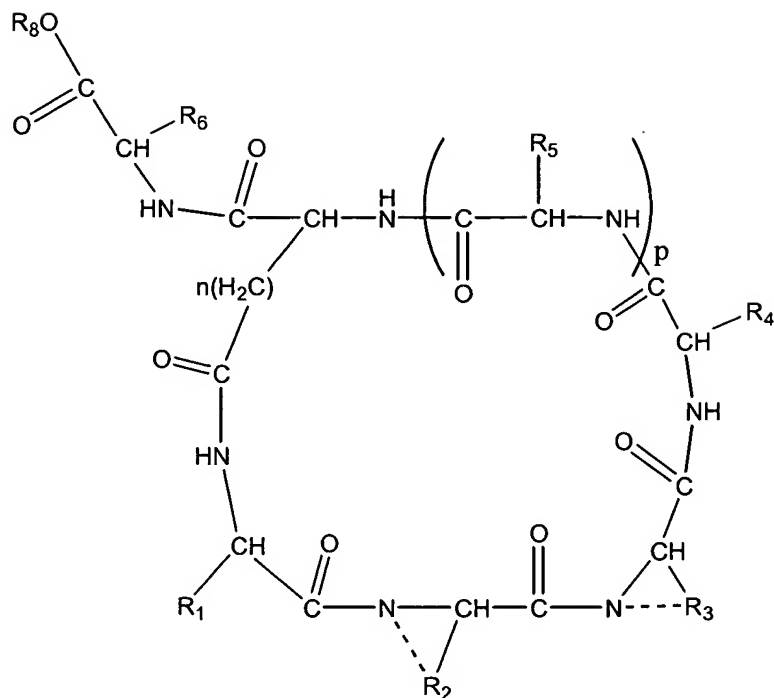
H-Gly-D-Dab-Gly-D-Hyp-D-Pro-D-Tyr

H-Gly-D-Dab-D-Ala-Gly-D-Hyp-D-Pro-D-Tyr

H-Gly-D-Dapa-D-Ala-Gly-D-Hyp-D-Pro-D-Tyr

And or pharmaceutically acceptable salts thereof.

90 (currently amended). ~~The~~ A compound according to claim 41 of formula XII further characterised by the general formula XV



92 (currently amended). ~~The~~A compound according to any one of the two preceding claims 90, wherein R₄ and R₅ are different or the same and represent the amino acid side chain of Gly or Ala.

93 (currently amended). ~~The~~A compound according to ~~any one of the three preceding claims~~ 90, wherein R₂ and R₃ represent together with the attached C and N atoms Pro or Hyp.

94 (currently amended). ~~The~~A compound according to ~~any one of the four preceding claims~~ 90, wherein R₁ represents Tyr.

95 (currently amended). ~~The~~A compound according to ~~any one of the five preceding claims~~ 90, wherein p is 1.

96 (currently amended). ~~The~~A compound according to ~~any one of the six preceding claims~~ 90, wherein n is 1.

97 (currently amended). ~~The~~ A compound according to claim 90 of formula XV selected from the group consisting of

(SEQ ID NO: 250)

Tyr-Pro-Hyp-Gly-Glu-Gly-NH₂

(SEQ ID NO: 251)

Tyr-Pro-Hyp-Gly-Asp-Gly-NH₂

(SEQ ID NO: 252)

Tyr-Pro-Hyp-Gly-Ala-Asp-Gly-NH₂

(SEQ ID NO: 253)

Tyr-Pro-Hyp-Gly-Ala-Glu-Gly-NH₂

D-Tyr-D-Pro-D-Hyp-Gly-D-Glu-Gly-NH₂

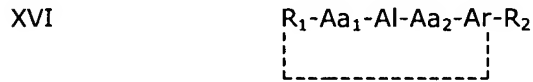
D-Tyr-D-Pro-D-Hyp-Gly-D-Asp-Gly-NH₂

D-Tyr-D-Pro-D-Hyp-Gly-D-Ala-D-Asp-Gly-NH₂

D-Tyr-D-Pro-D-Hyp-Gly-D-Ala-D-Glu-Gly-NH₂

and/or pharmaceutically acceptable salts thereof.

98 (currently amended). ~~A peptide~~A compound, wherein the amino acid residues may be L- and/or D-forms, and having the general formula XVI



Wherein R_1 represents an optional amide bond between the N and the C terminal of the peptide, H or Ac;

Aa_1 represents a peptide sequence of between 0 and 4 amino acid residues;

Al represents an amino acid residue selected from the group consisting of Gly, beta Alanine and Sar;

Aa_2 represents an amino acid residue selected from the group consisting of Asn, Gln, Gly, Tyr, or a chemical unit, such as a hydroxy acid, an amino sulphonic acid, a phosphate group or a hydrocarbon chain connecting G and Ar via 4 covalent bonds;

Ar represents an aromatic amino acid residue, such as a Tyr, Trp, Phe, His, or Nal, optionally substituted with one or more substituents selected from the group consisting of halogen, such as F, Cl, Br, or I, OH, NO₂, NH₂, COOH, and CONH;

R_2 represents OH, NH₂ or is missing;

and retro analogues, retro all-D analogues (retro-inverse analogues) and salts thereof.

99 (currently amended). ~~The~~A compound according to the preceding claim 98, wherein Aa_1 is selected from the group consisting of Ala, Gly-Ala, Gly-Asn-Tyr, and Gly-Asn-Tyr-Ala a portion of various listed compounds.

100 (currently amended). ~~The~~A compound according to any one of the two preceding claims 98, wherein Al represents Gly or Sar.

101 (currently amended). ~~The~~A compound according to any one of the three preceding claims 98, wherein Aa_2 represents Asn or Gln.

102 (currently amended). ~~The~~A compound according to any one of the four preceding claims 98, wherein Ar represents Tyr or Phe optionally substituted with one or more halogen, such as I.

103 (currently amended). ~~The~~A compound according to ~~any one of the five preceding claims 98~~, wherein R₂ represents -NH₂ when the compound is non-cyclic or R₂ is missing when the compound is cyclic.

104 (currently amended). ~~The~~A compound according to claim 98, ~~of formula XVI~~ selected from the group consisting of

(SEQ ID NO; 254) H-Gly-Ala-Gly-Asn-Tyr-NH₂,

(SEQ ID NO; 255) cyclo(-Tyr-Ala-Ser-Ala-Gly-Asn-),

(SEQ ID NO; 256) cyclo(-Tyr-Ala-Ser-Ala-Gly-Asn-),

(SEQ ID NO; 257) cyclo(-Tyr-Gly-Asn-Tyr-Ala-Gly-Asn-),

(SEQ ID NO; 258) cyclo(-Tyr-Val-Ser-Gly-Ala-Gly-Asn-),

Ac-Gly-Asn-Tyr-NH₂,

H-Gly-Asn-Tyr-NH₂,

(SEQ ID NO; 259) Ac-Ala-Gly-Asn-Tyr-NH₂,

(SEQ ID NO; 260) H-Ala-Gly-Asn-Tyr-NH₂, and pharmaceutically acceptable salts thereof.

105 (original). A photo labile derivative of a compound of formula I, XII, XIII, XIIIa, XIV, XV or XVI herein, characterised in having covalently bound to the N-terminal N atom a photo probe selected from the group consisting of azido, diazo compounds including diazirines and thiadiazoles, optionally substituted nitrophenyl, and optionally substituted benzophenones.

106 (currently amended). ~~The~~A compound according to ~~the preceding claim 105~~ selected from the group consisting of
Compound 31, 32, 33, 34 and salts thereof.

107 (currently amended). ~~A~~A thermo labile derivative of a compound of formula I-, XII, XIII, XIIIa, XIV, XV or XVI herein, characterised in having covalently bound to the N-terminal N atom a thermo probe selected from the group consisting of maleimido, optionally substituted pyridyl disulphides, optionally substituted aliphatic halides, isothiocyanates and isocyanates, carbodiimides, activated esters, such as N-hydroxysuccinimide.

108 (currently amended). A compound according to ~~the preceding claim 107~~, which is BrCH₂CO-Gly-Asn-Tyr-NH₂ and salts thereof.

109 (currently amended). A compound according to formulae I, XII, XIII, XIIIa, XIV, XV or XVI, ~~any one of the preceding claims~~, having an ~~which shows~~ antiarrhythmic effect in the

Langendorf model ~~described herein~~ when used in a concentration of from of 10^{-13} to 10^{-7} M, or preferably in a concentration range of 10^{-12} to 10^{-9} M when diluted in medium.

110 (currently amended). A pharmaceutical composition comprising a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI and formulae 2-12 or according to any one of the preceding claims, and a pharmaceutically acceptable carrier or diluent.

111 (currently amended). ~~The~~ A composition according to the preceding claim 110, which is an enteric tablet.

112 (currently amended). ~~A~~The composition according to claim ~~110~~111, which is an injection preparation.

113 (currently amended). A method of increasing the gap junctional intercellular communication of mammalian cells subjected to glucose and/or oxygen deprivation comprising administering an effective amount of a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI and formulae 2-12 or according to any one of claims ~~1-109~~ to said cells.

114. - 137. (cancelled)

138 (currently amended). A method of ~~treatment of~~ ment of arrhythmia comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI and formulae 2-12 or according to any one of claims ~~1-109~~.

139 (currently amended). ~~The~~A method of treatment according to the preceding claim 138, wherein said arrhythmia is a reentry arrhythmia of either atrial or ventricular origin, including repolarisation alternans arrhythmia where both supraventricular and ventricular tachyarrhythmias may present as tachycardia, flutter or fibrillation comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI, formulae 2-12 or according to any one of claims ~~1-109~~.

140 (currently amended). ~~A~~A method of antithrombotic treatment comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formula I, XII, XIII, XIIIa, XIV, XV or XVI or according to any one of claims ~~1-109~~.

141 (currently amended). A method of treatment of osteoporosis comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI, formulae 2-12, ~~or according to any one of claims 1-109.~~

142 (currently amended). A method of treating or preventing bone loss and increase the healing of bone fractures comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formula I, XII, XIII, XIIIa, XIV, XV or XVI, ~~or according to any one of claims 1-109.~~

143 (currently amended). A method of treatment of joint diseases including arthritis comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI, formulae 2-12, ~~or according to any one of claims 1-109.~~

144 (currently amended). A method of treatment of cancer in tissue of endodermal, mesodermal or ectodermal origin, including carcinomas and hepatocellular and cholangiocellular neoplasms and bone cancer comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI, formulae 2-12 ~~or according to any one of claims 1-109.~~

145 (currently amended). A method of treatment wounds and in particular ischemic ulcers comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI, formulae 2-12, ~~or according to any one of claims 1-109.~~

146 (currently amended). A method of treatment gastric and duodenal ulcers comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI, formulae 2-12, ~~or according to any one of claims 1-109.~~

147 (currently amended). A method of treating or preventing hypertension by increasing gap junctional coupling and/or GJIC in the vascular wall comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formula I, XII, XIII, XIIIa, XIIIa, XIV, XV or XVI, ~~or according to any one of claims 1-109.~~

148 (currently amended). A method of preventing ischemic damage in the brain and treating organic psychoses that may present with symptoms such as depression, anxiety, learning and memory deficit, fobias, or hallucinations comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI, formulae 2-12, ~~or according to any one of claims 1-109.~~

149 (currently amended). A method of treating or preventing cataract comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI, formulae 2-12, ~~or according to any one of claims 1-109.~~

150 (currently amended). A method of treatment of deafness associated with impaired GJIC comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI, formulae 2-12, ~~or according to any one of claims 1-109.~~

151 (currently amended). A method of treatment of gastrointestinal motility disorders comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI, formulae 2-12, ~~or according to any one of claims 1-109.~~

152 (currently amended). A method of treatment of female infertility that is due to poor cell-to-cell coupling in the ovaries comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI, formulae 2-12, ~~or according to any one of claims 1-109.~~

153 (currently amended). A method of induction of and facilitation of labour comprising administering along with oxytocin to a patient in need of such treatment a therapeutically effective amount of a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI, formulae 2-12, ~~or according to any one of claims 1-109.~~

154 (currently amended). A method of treatment of male infertility associated with impaired cell-to-cell coupling comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI, formulae 2-12, ~~or according to any one of claims 1-109.~~

155 (currently amended). A method of improving glucose tolerance in a subject with non-insulin dependent diabetes mellitus due to impaired GJIC between β -cells comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formulae I, XII, XIII, XIIIa, XIV, XV and XVI, formulae 2-12, ~~or according to any one of claims 1-109.~~

156 (currently amended). A method of treating or preventing disease in poorly vascularized cartilage and joints comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formula I, XII, XIII, XIIIa, XIIIa, XIV, XV or XVI, ~~or according to any one of claims 1-109.~~

157 (currently amended). ~~The~~A method according to the preceding claim 156, wherein said disease is arthritis.

158 (currently amended). A method of treating or preventing cataract comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formula I, XII, XIII, XIIIa, XIIIa, XIV, XV or XVI, ~~or according to any one of claims 1-109.~~

159 (currently amended). A method of treating or preventing vascularization of the cornea in disease states with poor nutrition of the cornea and increase the healing of corneal lesions comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formula I, XII, XIII, XIIIa, XIIIa, XIV, XV or XVI, ~~or according to any one of claims 1-109.~~

160 (currently amended). A method of treating or preventing growth and spreading of cancer cells comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of formula I, XII, XIII, XIIIa, XIIIa, XIV, XV or XVI, ~~or according to any one of claims 1-109.~~

161 (currently amended). A method of treatment of glucose and oxygen deprivation of cells, a tissue, or an organ in a patient suffering therefrom comprising administering to said patient an effective amount of a compound of formula I, XII, XIII, XIIIa, XIIIa, XIV, XV or XVI, ~~or according to any one of claims 1-109.~~

162 (currently amended). TheA method according to the preceding claim, wherein said organ is the heart.